110. E. E. Smissman and M. Steinman, J. Med. Chem., 9, 455 (1966).
111. D. V. Sokolov, K. D. Praliev, P. T. Sydykov, B. I. Artyukhin, D. M. Manatadov, V. M. Kurilenko, Zh. N. Khlienko, and L. M. Moiseeva, in: Summaries of Papers Presented at the All-Union Conference on the Synthesis and Mechanism of the Action of Physiologically Active Substances [in Russian], Odessa (1976), p. 13.
112. M. Prost, M. Urbain, A. Schumer, V. Van Cromphaut, C. Houben, C. Van Meerbeeck, M. Colot, and R. Charlier, Eur. J. Med. Chem., 11, 337 (1976).
113. B. B. Kuz'mitskii, A. A. Akhrem, L. I. Ukhova, and N. F. Uskova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2774 (1970).
114. V. V. Gavrilova, V. E. Golender, A. B. Rozenblit, N. M. Sukhova, M. Yu. Lidak, and É. Ya. Lukevits, Khim.-farm. Zh., 13, 45 (1979).
115. V. V. Drboglav, V. P. Golubovich, L. I. Ukhova, A. A. Akhrem, V. E. Golender, and A. B. Rozenblit, Khim.-farm. Zh., 6, 581 (1982).

METHOD FOR THE SYNTHESIS OF BISBENZO[c]PYRYLIUM SALTS

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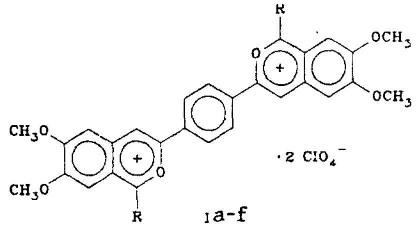
A new method for the synthesis of bisbenzo[c]pyrylium salts was developed. The new method is based on the acylation of 1,4-bis(3,4-dimethoxyphenylacetyl)benzene with carboxylic acid anhydrides in the presence of perchloric acid or with carboxylic acids in polyphosphoric acid.

Owing to their ability to undergo recyclization under the influence of nucleophilic reagents, benzo[c]pyrylium salts are of interest as intermediates for the synthesis of a large number of heterocyclic and aromatic compounds [1]. Benzo[c]pyrylium salts are obtained most readily via the reaction in [2], which consists in catalytic acylation with subsequent heterocyclization of ring-activated arylacetones and deoxybenzoins. The use of dibasic aliphatic acids with no less than three carbon atoms between the carboxy groups as the acylating agents in the indicated reaction made it possible to synthesize the previously unknown bisbenzo[c]pyrylium salts; some of them served as the basis for obtaining analogs of the natural alkaloid dauricine [3, 4].

We have developed a new variant of the synthesis of compounds, the molecules of which contain two pyrylium cations, viz., p-phenylenebis(1-R-6,7-dimethoxybenzo[c]-3-pyrylium) diperchlorates I.



Ia-f

I a R=H; b R=CH$_3$; c R=C$_2$H$_5$; d R=CH$_2$C$_6$H$_5$; e R=C$_6$H$_5$; f R=4-OCH$_3$—C$_6$H$_4$

The proposed method consists in acylation of 1,4-bis(3,4-dimethoxyphenylacetyl)benzene (II) with carboxylic acid anhydrides in the presence of perchloric acid or with carboxylic acids in polyphosphoric acid (PPA). The presence in starting substrate II of two aromatic rings that are activated to electrophilic attack makes it possible to avoid the limitations that are imposed in known methods [3, 4] on the structure of the acylating agents and to use a more extensive series of accessible monobasic aromatic and aliphatic acids and their anhydrides to obtain the bisbenzo[c]pyrylium salts.

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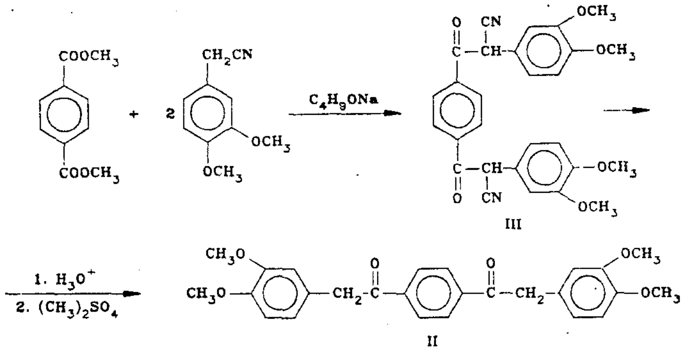
Diketone II was obtained by acidic hydrolysis of bis(β-keto nitrile) III — the product of condensation of dimethyl terephthalate with 3,4-dimethoxyphenylacetonitrile.

Sodium butoxide, which was obtained by azeotropic distillation of the water from a mixture of sodium hydroxide, butanol, and xylene, was used as the condensing agent. The IR spectrum of crude keto nitrile III contains intense absorption bands of conjugated nitrile groups at 2210 cm^{-1} and of double bonds at 1645 cm^{-1}; this indicates significant enolization. The subsequent transformations of keto nitrile III were carried out without additional purification. Its hydrolysis under the influence of sulfuric acid led to a product that was completely soluble in water; this was evidently a consequence of sulfonation of the dimethoxyphenyl rings. The use of hydrochloric acid was more successful, but the reaction was complicated in this case also by splitting out of methoxy groups; this made it necessary to additionally treat the hydrolysis product with dimethyl sulfate. The overall yield of diketone II was 28%. The same result was also obtained when sodium hydride was used as the condensing agent (with dimethoxyethane as the solvent).



The synthesis of bisbenzo[c]pyrylium salt Ia, which does not have substituents in the 1 and 1' positions, was realized by formylation of diketone II with dichloromethyl butyl ether in the presence of aluminum chloride. The use of acetic and propionic acid anhydrides as the acylating agents in the presence of equimolar amounts of perchloric acid gives diperchlorates Ib, c. Salts Id-f were obtained by heating diketone II with, respectively, phenylacetic, benzoic, and anisic acids in polyphosphoric acid (PPA). The resulting chloroaluminate (Ia) and phosphates (Id-f) were converted to the more stable perchlorates.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in CF_3COOH were recorded with a Tesla BS-467 spectrometer (60 MHz) with tetramethylsilane (TMS) as the internal standard.

1,4-Bis(3,4-dimethoxyphenylacetyl)benzene (II). A mixture of 75 ml of n-butanol, 105 ml of xylene, and 6 g (150 mmole) of sodium hydroxide was refluxed with a Dean—Stark trap until water separation ceased. A 12-g (60 mmole) sample of dimethylterephthalate and 43.5 g (240 mmole) of 3,4-dimethoxyphenylacetonitrile were added to the resulting solution of sodium n-butoxide, and the mixture was refluxed with removal of the solvent by distillation until 150 ml of distillate had been collected. The cooled residue was dissolved in 1 liter of water, and the solution was extracted with benzene (three 100-ml portions). The aqueous layer was acidified with hydrochloric acid, and the precipitate was removed by filtration, washed with water until the wash water was neutral, and dried. The dry precipitate (24.5 g) was mixed with 200 ml of acetic acid and 200 ml of concentrated HCl, and the mixture was refluxed for 5 h. The solution was diluted with 1.5 liters of water, and the resulting precipitate was removed by filtration and washed with water until the wash water was neutral. The squeezed moist precipitate was introduced into a solution of 15 g of sodium hydroxide in 200 ml of water, and the mixture was treated with stirring with 28 ml of dimethyl sulfate, after which the mixture was heated for 30 min on a boiling-water bath. It was then cooled, and the precipitate was removed by filtration, washed with water, and dried to give 7.5 g (28%) of a product with mp 156-158°C. IR spectrum: 1690 cm^{-1} (C=O). Found: C 71.7; H 6.2%. $C_{26}H_{26}O_6$. Calculated: C 71.9; H 6.0%.

p-Phenylenebis(6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (Ia). A 2.7-g (20 mmole) sample of aluminum chloride was added to a stirred solution of 2.15 g (5 mmole) of diketone

II in 15 ml of methylene chloride with cooling with ice water, after which 3.14 g (20 mmole) of dichloromethyl butyl ether was added dropwise, and the reaction mass was stirred with cooling for 30 min and at 20°C for 1 h, after which it was poured into a mixture of ice and hydrochloric acid. The resulting precipitate was removed by filtration and washed successively with a mixture of equal volumes of isopropyl alcohol and ether and with ether. The precipitate was mixed with 5 ml of nitromethane, 1.5 ml of 70% perchloric acid was added, and the mixture was heated until the precipitate dissolved. The solution was then cooled and diluted with ether, and the precipitate was removed by filtration to give 2.3 g (70%) of a product with mp 249-250°C (dec.). PMR spectrum: 4.17 (6H, s, two OCH_3); 4.33 (6H, s, two OCH_3); H_{arom}: 7.67 (2H, s); 7.73 (2H, s); 8.43 (4H, s); 8.67 (2H, s); 9.80 ppm (2H, s). Found: C 50.9; H 4.0; Cl 10.4%. $C_{28}H_{24}Cl_2O_{14}$. Calculated: C 51.3; H 3.7; Cl 10.8%.

p-Phenylenebis(1-methyl-6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (Ib). A solution of 2.15 g (5 mmole) of diketone II in 30 ml of nitromethane was added dropwise with stirring to a solution of 1.6 ml of 70% perchloric acid in 20 ml of acetic anhydride. After 30 min, the thickened reaction mass was diluted with ether, and the precipitate was removed by filtration and dried to give 3.1 g (90%) of a product with mp 285°C (dec.). PMR spectrum: 3.45 (6H, s, two CH_3); 4.25 (6H, s, two OCH_3); 4.35 (6H, s, two OCH_3); H_{arom}: 7.67 (2H, s); 7.72 (2H, s); 8.42 (4H, s); 8.57 ppm (2H, s). Found: C 53.0; H 3.7; Cl 10.7%. $C_{30}H_{28}Cl_2O_{14}$. Calculated: C 52.7; H 4.1; Cl 10.4%.

p-Phenylenebis(1-ethyl-6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (Ic). This compound was obtained from diketone II and propionic anhydride by a procedure similar to that used to obtain Ib. The product, with mp 248-250°C (dec.), was obtained in 71% yield. PMR spectrum: 1.66 (6H, t, two CH_3); 3.63 (4H, q, two CH_2); 4.00 (6H, s, two OCH_3); 4.10 (6H, s, two OCH_3); H_{arom}: 7.30 (2H, s); 7.37 (2H, s); 8.00 (4H, s); 8.10 ppm (2H, s). Found: C 53.5; H 4.9; Cl 10.1%. $C_{32}H_{32}Cl_2O_{14}$. Calculated: C 54.0; H 4.5; Cl 10.0%.

p-Phenylenebis(1-benzyl-6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (Id). A solution of 2.15 g (5 mmole) of diketone II and 4 g (30 mmole) of phenylacetic acid in 100 g of polyphosphoric acid (PPA) was stirred at 100°C for 2 h, after which the hot reaction mass was poured into water, and perchloric acid was added until the formation of a yellow precipitate was complete. The precipitate was removed by filtration, washed with isopropyl alcohol and ether, and dried to give 3.2 g (75%) of a product with mp 275-276°C (dec.). PMR spectrum: 4.05 (6H, s, two OCH_3); 4.20 (6H, s, two OCH_3); 4.95 (4H, s, two CH_2); H_{arom}: 7.35 (10H, s); 7.52 (2H, s); 7.72 (2H, s); 7.95 (4H, s); 8.38 ppm (2H, s). Found: C 60.9; H 4.5; Cl 8.3%. $C_{42}H_{36}Cl_2O_{14}$. Calculated: C 60.4; H 4.3; Cl 8.5%.

p-Phenylenebis(1-phenyl-6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (Ie). This compound was obtained from diketone II and benzoic acid by a procedure similar to that used to obtain Id. For conversion to the perchlorate, phosphate Ie was mixed with nitromethane, excess perchloric acid was added, the the mixture was heated until dissolving was complete. The solution was cooled and diluted with ether, and the precipitate was removed by filtration to give a product with mp 295-297°C (dec.) in 60% yield. PMR spectrum: 3.87 (6H, s, two OCH_3); 4.10 (6H, s, two OCH_3); 7.27-8.17 ppm (20H, m, H_{arom}). Found: C 59.8; H 4.3; Cl 8.6%. $C_{40}H_{32}Cl_2O_{14}$. Calculated: C 59.5; H 4.0; Cl 8.8%.

p-Phenylenebis[1-(4-methoxyphenyl)-6,7-dimethoxybenzo[c]-3-pyrylium) Diperchlorate (If). This compound was obtained from diketone II and anisic acid by a procedure similar to that used to obtain Ie. The yield of product with mp 286-288°C (dec.) was 78%. PMR spectrum: 3.87 (6H, s, two OCH_3); 3.92 (6H, s, two OCH_3); 4.10 (6H, s, two OCH_3); H_{arom}: 7.16 (4H, d, J = 9 Hz); 7.47 (2H, s); 7.67 (2H, s); 7.96 (4H, d, J = 9 Hz); 8.20 (4H, s); 8.27 ppm (2H, s). Found: C 57.7; H 4.4; Cl 8.4%. $C_{42}H_{36}Cl_2O_{16}$. Calculated C 58.1; H 4.2; Cl 8.2%.

LITERATURE CITED

1. G. N. Dorofeenko, E. I. Sadekova, and E. V. Kuznetsov, The Preparative Chemistry of Pyrylium Salts [in Russian], Izd. Rostovsk. Gosudarstv. Univ., Rostov-on-Don (1972).
2. Ya. P. Stradyn', Khim. Geterotsikl. Soedin., No. 10, 1412 (1981).
3. G. N. Dorofeenko, E. V. Kuznetsov, and E. I. Sadekova, Khim. Geterotsikl. Soedin., No. 4, 454 (1972).
4. G. N. Dorofeenko and E. I. Sadekova, Khim. Prir. Soedin., No. 5, 714 (1977).